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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/297,092	05/18/1999	MICHAEL PAULISTA	P564-9010	9258

6449 7590 09/16/2004

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EXAMINER	
KAUSHAL, SUMESH	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 09/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/297,092	PAULISTA ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-25,28,30,32 and 33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-25, 28, 30 and 32-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 06/30/04 has been acknowledged.
Claims 17-25, 3 and, 32-33 are pending and are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is ***703-872-9306****.*

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 06/30/04 has been entered.

Claim Rejections - 35 USC § 112

Claims 17-25, 28, 30 and 32-33 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to

make and/or use the invention for the same reasons of record as set forth in the office action mailed on 06/24/04.

Nature of Invention:

Invention relates to a method of treating bone defects and an implant material suitable for cartilage, bone or cartilage and bone growth comprising crystallographically phase-pure calcium phosphate and fragments of MP52 protein (as claimed).

Breadth of Claims and Guidance Provided in the Specification:

The instant claims are drawn to an implant for cartilage and/or bone growth comprising a crystallographically phase-pure calcium phosphate matrix and a cartilage and/or bone inducing MP52 protein or DNA encoding the MP52 protein, wherein the MP52 protein is selected from the group consisting of fragments of SEQ ID No:1 comprising amino acid 1 to 501 , 28 to 501 , 361-400 to 501, 381 to 501 and 382 to 501 of SEQ ID NO. 1. The instant claims are further drawn to a method of treating a disease, which affect cartilage and/or bone and/or damage to cartilage and/or bone in a patient by implanting the implant material as claimed.

The specification states that many members of TGF-beta, BMP and GDF subfamilies have cartilage and/or bone inducing potentials. The specification further states that it can be assumed that a combination of various factors would be advantageous for the efficiency of cartilage and bone induction (spec. page 3, para.1). The specification further teaches the use of crystallographically phase-pure alpha and beta tricalcium phosphate ceramics in making of the implant as claimed (spec. 13, para.1). In addition the specification suggested that the efficacy of the implant material could be tested in conventional test systems such as animal models (spec. page 19-20). However, the instant specification fails to disclose that the implantation of the implant material (as claimed) leads to bone or cartilage formation in any and all animals. The specification even fails to provide any evidence that a protein encoded by SEQ ID NO:1 or any fragment thereof (as claimed) have any bone and/or cartilage inducing activity in-vivo.

State of Art and Predictability

The state of the art at the time of filing teaches that the signal transduction mechanism of members of TGF-beta superfamily is complex and the members are know to regulate plethora of developmental processes (Attisano et al, Science. 296:1646-1647, 20002). For example, proteins of the TGF-beta superfamily bind to two different types of signaling receptors termed as type II and type I receptors. Upon ligand binding and formation of type II and type I receptor complexes, followed by possible receptor conformational changes, type I receptors are phosphorylated and activated by type II receptor kinases. Type I receptor kinases then transmit intracellular signals by phosphorylating Smad proteins. In mammals, only five type II receptors and seven type I receptors have been identified. It is theoretically possible to form more than 30 different combinations of type II and type I receptors. However, certain type II receptors tend to interact with certain type I receptors. Thus, the combinations of type II and type I receptors appear to be limited under physiological conditions and the variety of ligands converges at the receptor level (Miyazono et al, J Cell Physiol, 187(3):265-76, 2001). The instant specification fails to disclose that MP52 modulates bone and/or cartilage formation. In addition, the specification fails to disclose what are another dimmer of TGF-beta superfamily that in combination with MP52 that would leads to cartilage and/or bone formation.

Furthermore, it is general knowledge in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity if amino acids that are critical for such functions are substituted, and the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable. The recited fragment of SEQ ID NO:1 are mere hypothetical fragments since the specification fails to disclose that these fragments possess any bone or cartilage formation activity. In addition, mere identification of critical regions would not be sufficient, as the ordinary artisan would immediately recognize that the encoded polypeptide must assume the proper three-dimensional configuration to be active, which is dependent upon the surrounding residues. Thus, in order to elucidate the roles of TGF-beta and a morphogenetic protein in clinical disorders it is very important to

understand the signaling mechanisms of those proteins in vivo (see Miyazono, page 272, conclusion).

It is noted that patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.

In instant case use of any fragment of MP52 protein (as claimed) for the treatment of any bone or cartilage defect is not considered routine in the art and without sufficient guidance to a specific therapeutic gene the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). Thus, in view of lack of specific guidance in the specification, the skilled artisan at the time of filing would be unable to use the invention as claimed, without an excessive and undue amount of experimentation. The quantity of experimentation required would include making an implant as claimed, containing fragments of MP52 protein (as claimed) and testing the implant for bone and/or cartilage inducing activity in-vivo for the treatment of any bone defect, bone fracture, modification of jaw region (as claimed) and periodontosis.

Conclusion

No claims are allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 571-272-0781.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to ***(571) 272-0547.*** For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **703-872-9306.**

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image

problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

Sumesh Kaushal
Examiner GAU 1636

JEFFREY FREDMAN
PRIMARY EXAMINER
9/14/04